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EDITORIAL COMMENT

Which Measures of Obesity Best Predict Cardiovascular Risk?*

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> *"The possible relationship between obesity and cardiovascular disease has been the subject of great controversy."* (1)

In the 24 years since this statement was written, the contentiousness over the issue has evolved somewhat, but has not abated. Today, there is general acceptance that obesity is a risk factor for cardiovascular disease (CVD). However, we now have difficulty in reaching a consensus on the definition of obesity or on which specific aspects of obesity contribute to CVD. The major disagreement centers on the topic of whether the total amount or the distribution of adipose tissue confers the greater risk of developing CVD. One paradigm holds that generalized obesity, usually assessed by the body mass index (BMI) expressed in kg/m^2, adequately predicts the development of CVD or CVD-associated death (2–12). The other school is entrenched in the belief that central or abdominal obesity is the key abnormality leading to cardiovascular pathology (13–16). According to the latter theory, visceral fat, via a variety of mechanisms, is proatherogenic, but subcutaneous and/or peripheral fat is not (17–25). Proponents of the central obesity hypothesis correctly point out that BMI misclassifies some people as being normal weight or obese (26). The extent to which such misclassification occurs in large populations is unclear because waist circumference and BMI correlate closely (26,27).

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Determining the best method for quantifying adiposity is important because this may: 1) define higher- and lower-risk subgroups of patients that require different levels of treatment intensity (i.e., deciding when to aim for lower target low-density lipoprotein cholesterol levels) (28); and 2) reveal insights into the mechanisms by which obesity is linked to cardiovascular maladies.

The World Health Organization has defined overweight and class I to III obesity based on BMI. This metric is very easy to obtain, reproducible, unambiguous, and widely accepted and understood. Despite the relative crudeness of the measure, in population studies including almost 3.5 million people, increased BMI has consistently been shown to predict total and cardiovascular mortality (2–12). The relative risk of cardiovascular mortality in the highest BMI groups has been reported to be 2 to 4 times that of the normal weight group in nearly all of the largest studies. The prevalence of overweight and obesity as defined by BMI is rapidly increasing, particularly in children and adolescents (29). At the same time, we are seeing an increase in the severity of coronary disease in younger people (30). This has occurred despite increased use of evidence-based treatments for hypertension and hyperlipidemia (31). Even more ominous, with the increasing prevalence of obesity, there appears to be a reversal of the 2-decade-long decline in death rates from CVD (32).

Abdominal obesity is a central component of the metabolic syndrome and is thought to play a specific role in insulin resistance and dyslipidemia (21). Given this, it is not surprising that larger waist circumferences may be associated with a higher risk of developing CVD or cardiovascular mortality. Interestingly, larger hip circumferences, suggesting peripheral fat deposition, have been associated with less severe CVD risk factors or a lower risk of incident CVD (33–35). Because of the opposing effects of waist and hip circumferences, the waist-to-hip ratio has become a popular method of assessing atherogenic risk. Indeed, in a number of studies the waist-to-hip ratio performed better than waist circumferences in predicting CVD (1,36–40). The adherents of the visceral fat theory generally advocate obtaining measures of central obesity such as waist circumference or a direct measure of visceral fat obtained with computed tomography or magnetic resonance imaging. These measures, though appealing, have not been validated as extensively as BMI. In addition, there is no clear consensus on how (or where) to measure these parameters or on defining the optimal cutoff values for normal and abnormal. The debate over how to best define obesity is complicated by observations suggesting that BMI, waist circumference, or waist-to-hip ratio may each perform better in predicting cardiovascular risk in specific populations, depending on gender, age, and ethnicity. For example, in older patients, BMI is less robust at predicting an increased relative risk of CVD-related mortality even though higher BMI is strongly related to increased absolute mortality in the elderly (11,41). Although it has not been examined rigorously, there is some suggestion in the existing literature that BMI is a less robust predictor of CVD than waist circumference in women but not in men (9,15). The "android" pattern of obesity (central obesity) is less common in women, and thus, increased waist circumference might confer a higher relative risk in women than in men.

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Two recent studies readdress the topic and reach different conclusions. Zhang et al. (26) calculated total and cause-specific mortality in a subset of patients from the Nurse's Health Study (42). Their analysis included 44,636 participants who reported waist circumference on the 1986 questionnaire (from the initial cohort of 115,195 subjects enrolled in 1976). They found correlation coefficients of 0.81 and 0.96 between waist circumference and BMI or waist/height, respectively. Their main conclusion was that measures of abdominal obesity were strongly and positively associated with all-cause and cardiovascular mortality independently of BMI. The relative risk of age-adjusted CVD mortality was 2.02 for the highest versus the lowest quintiles of waist circumference. Furthermore, they found that elevated waist circumference was associated with increased cardiovascular mortality even in normal weight women. Interestingly, an earlier report that included data from the entire cohort enrolled in the Nurse's Health Study found that women with a BMI $\geq$32 kg/m^2 and who had never smoked had a 4.1-fold increase in the relative risk of death from CVD (7). The earlier report indicated that lean women did not have excess mortality.

In this issue of the *Journal,* Gelber et al. (27) analyze existing data from 2 large clinical trials—the Physician's Health Study (43) and the Women's Health Study (44). These investigators conclude that BMI is clinically equivalent to waist circumference in predicting major CVD events or death. The results of the current study may not resolve the controversy, but do provide some practical suggestions about the most useful way to define obesity. The large size of the cohorts in this study (more than 49,000 participants), the inclusion of both men and women, the relatively long duration of follow-up (9 years for the Physician's Health Study and 6 years for the Women's Health Study), the significant number of adjudicated hard end points (1,505 cases of first nonfatal myocardial infarction, nonfatal ischemic stroke, or cardiovascular death), and the adjustment for multiple relevant covariates strengthen the conclusions of this study. The main findings were that all measures of adiposity (BMI, waist circumference, waist-to-hip ratio, and waist-to-height ratio [WHtR]) correlated with each other (r values of ~0.8) and with incident CVD. Although WHtR had the strongest gradient in the association with incident CVD (e.g., a greater relative risk for each increment of the various anthropometric variables), the investigators concluded that "differences between BMI and WHtR in association with CVD… [are] small and likely not clinically consequential." Furthermore, they assert, "BMI may remain the most clinically practical measure of adiposity" (27).

I find these conclusions to be refreshing. Clinical practicality is frequently overshadowed by statistical significance. Many readers of this journal are all too familiar with the realities of struggling to move patients efficiently through our offices while still documenting all necessary bullet points, examining the patient, reviewing their test results, and spending time counseling them and answering questions. Do we really need multiple measures of body size or geometry to determine if our patient is overweight or obese? Will our patients tolerate having their waist and hip circumferences measured? The "eyeball test" is probably a reasonable method for assessing adiposity in most instances. Because quantitation of adiposity allows a more detailed risk assessment and allows comparison of changes over time, an unambiguous, simple parameter to support our visual and clinical assessment will be useful. The data shown by Gelber et al. (27) argue that BMI should be that single measure. Sure, there are patients in whom the BMI will give an inaccurate assessment of adiposity. For example, those with large body frames and heavy muscle mass may be incorrectly classified as obese, but at the other end of the spectrum, those with muscle wasting, yet still replete with adipose tissue could be classified as lean (particularly elderly subjects) (45). However, these are relatively small subsets of the patients we see in today's medical practices. Do we really need to measure waist *and* hip circumferences (with their inherent inaccuracies based on location of the measurement), or worse yet, perform routine abdominal computed tomography scans to identify the well-muscled football player or the elderly patient with little muscle mass but abdominal obesity? I think not.

The medical profession suffers in the eyes of the public because we bombard them with conflicting data and inconsistent conclusions. They grow confused and disillusioned with our controversies. Who among us has not been asked by our own friends and family whether they are better off eating a diet low in total fat, low in saturated fat, low in cholesterol, or low in carbohydrates? Can you give them a cogent answer? Let us not fall into the trap of uncertainty when it comes to discussing the topic of obesity. Given the importance of obesity as a public health issue, it behooves us to keep sight of the big picture. The obesity epidemic will likely bring an end to the steadily progressive increases in overall life expectancy that we have witnessed in our lifetimes (46). With no end in sight to the growing epidemic, obesity arguably poses the greatest challenge of any medical condition to worldwide health in the foreseeable future.

As medical professionals and scientists, let us speak with a united, unequivocal voice when we talk to our patients about obesity. We should not vacillate about how we measure or define obesity. There is no "good" fat—the fat cell is the enemy. This concept must be clear and simple when we address patients, friends, family, and the public. For the purposes of research, it is important to understand the pathophysiology of obesity-related CVD. To this end, teasing out the different subtypes, distributions, or patterns of obesity and their relation to CVD is a highly worthy goal. However, for the sake of our patients, we must stay on the message. All obesity is potentially deleterious. Regardless of how we define obesity, it is putting today's children at risk. The BMI is the simplest and most widely accepted measure of obesity. Few other

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indexes have been so extensively studied and validated. As a profession, we serve our patients and our communities best by singularly adopting this metric.

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